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Regioselective Transfer Hydrogenative Defluorination of Polyfluoroarenes Catalyzed by Bifunctional Azairidacycle

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Abstract: The catalytic hydrodefluorination (HDF) with a bifunctional azairidacycle using HCOOK was examined for cyano- and chloro-substituted fluoroarenes, including penta- and tetrafluorobenzonitriles, tetrafluoroterephthalonitrile, tetrafluorophthalonitrile, 3-chloro-2,4,5,6-tetrafluoropyridine, and 4-cyano-2,3,5,6-tetrafluoropyridine. The reaction was performed in the presence of a controlled amount of HCOOK with a substrate/catalyst ratio (S/C) of 100 in a 1:1 mixture of 1,2-dimethoxyethane (DME) and H_2O at an ambient temperature of 30 °C to obtain partially fluorinated compounds with satisfactory regioselectivities. The C–F bond cleavage proceeded favorably at the *para* position of substituents other than fluorine, which is in consonance with the nucleophilic aromatic substitution mechanism. In the HDF of tetrafluoroterephthalonitrile and 4-cyano-2,3,5,6-tetrafluoropyridine, which do not contain a fluorine atom at the *para* position of the cyano group, the double defluorination occurred solely at the 2- and 5-positions, as confirmed by X-ray crystallography. The HDF of 3-chloro-2,4,5,6-tetrafluoropyridine gave preference to the C–F bond cleavage over the C–Cl bond cleavage, unlike the dehalogenation pathway via electron-transfer radical anion fragmentation. In addition, new azairidacycles with an electron-donating methoxy substituent on the C–N chelating ligand were synthesized and served as a catalyst precursor (0.2 mol%) for the transfer hydrogenative defluorination of pentafluoropyridine, leading to 2,3,5,6-tetrafluoropyridine with up to a turnover number (TON) of 418.

Keywords: azairidacycle; bifunctional catalyst; cyclometalation; hydrodefluorination; nucleophilic aromatic substitution; transfer hydrogenation

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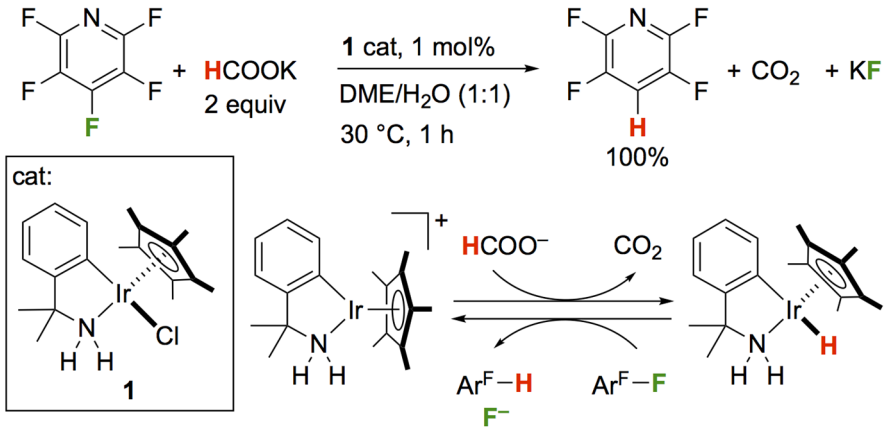
1. Introduction

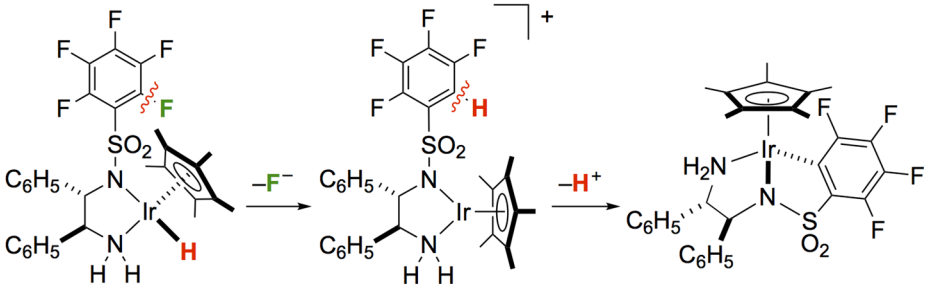
Fluorine containing organic compounds has been receiving much attention in the field of pharmaceuticals, agrochemicals, and functional materials. In general, perfluorinated aromatic compounds are practically obtained by fluorination of hydrocarbons using fluorine gas or hydrogen fluoride, whereas the synthesis of partially fluorinated compounds is still under development [1–3]. Aside from specific arene fluorinations using electrophilic, nucleophilic, or radical fluorine sources [4–10], hydrodefluorination (HDF) can be regarded as a valuable method, especially in the regioselective transformation of C–F bonds on perfluoroarenes [11–13]. Among the catalytic systems using transition metals, hazardous fluorophilic reductants such as hydrosilanes [14–23] and aluminum hydrides [24,25] have been widely used to facilitate the cleavage of strong C–F bonds. Hydrogenolysis of fluoroarenes has also been reported as an atom-economical HDF system [26–32].

As an alternative approach to avoid unsafe procedures, we have developed the HDF of perfluoroaromatic compounds promoted by an Ir-based transfer hydrogenation catalyst **1** using 2-propanol or formate salts as mild reducing agents (Scheme 1) [33,34]. A catalytically active hydridoiridium complex possessing a σ-donating aryl-metal bond and a protic

amine ligand engaged in the HDF at an ambient temperature of 30 °C, leading to an outstanding catalytic performance characterized by bifunctional amido/amine complexes. For example, pentafluoropyridine and monosubstituted pentafluorobenzenes were selectively defluorinated at the 4-position to give the corresponding HDF products in satisfactory yields. The reduction of fluorinated benzene derivatives was markedly facilitated by the introduction of electron-withdrawing substituents. These experimental results suggest a nucleophilic aromatic substitution (S_NAr) mechanism involving the powerful hydridoiridium species. Separately, we also investigated the stoichiometric C–F bond cleavage reactions of aromatic fluorides, illustrated by the related iridium complexes bearing fluorinated phenylsulfonyl-1,2-diphenylethylenediamine ligands [35–37]. The thermolysis of the isolable hydridoiridium revealed a successive conversion into iridacycles via intramolecular HDF caused by the nucleophilic attack of the hydrido ligand (Scheme 2) [35].



Scheme 1. Transfer hydrogenative defluorination catalyzed by azairidacycle **1**.



Scheme 2. Cyclometalation of hydridoiridium bearing *N*-pentafluorobenzenesulfonylated 1,2-diphenylethylenediamine via intramolecular hydrodefluorination.

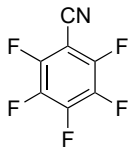
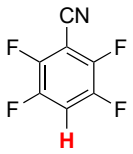
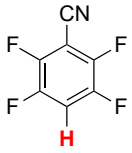
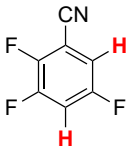
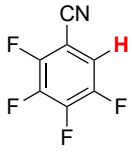
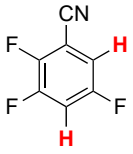
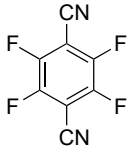
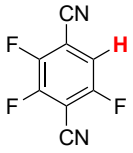
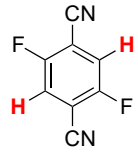
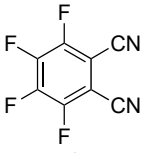
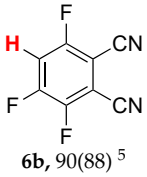
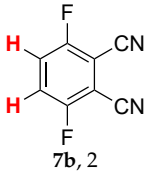
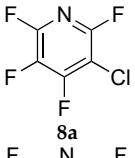
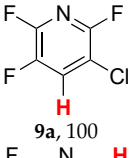
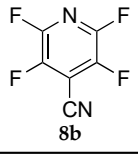
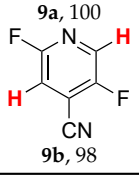
In order to reinforce the S_NAr mechanism [38,39] in the transfer hydrogenative defluorination catalyzed by **1**, we herein investigated the advanced control of the regio- and chemoselectivity by extension of the substrates, which can provide valuable insight into the hydride transfer process. On the basis of the aromatic C–F bond cleavage by Ir-bonded nucleophilic ligands, we also modified the azairidacycle catalyst to enhance the hydridicity via the introduction of an electron-donating methoxy substituent on the C–N chelating ligand. The influence of electronic tuning on the catalytic HDF performance is elucidated.

2. Results and Discussion

According to the transfer hydrogenation system promoted by the azairidacycle **1** [33], the HDF of selected polyfluoroarenes was performed with a substrate/catalyst molar ratio of 100 in a mixture of aqueous potassium formate and 1,2-dimethoxyethane. The results are summarized in Table 1. When pentafluorobenzonitrile (**2a**) was treated with 2 equiv of HCOOK at 30 °C for 1 h, the fluorine atom at the *para* position was substituted to

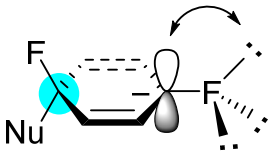
give 2,3,5,6-tetrafluorobenzonitrile (**3a**) in a quantitative yield (Entry 1). Even with the extra amount of the hydride source, a successive defluorination hardly proceeded. The further defluorination of **3a** with the elongation of the reaction time to 12 h resulted in the formation of 2,3,5-trifluorobenzonitrile (**4**) in a moderate yield of 20% (Entry 2). Notably, the same compound **4** was smoothly accessible via the HDF of 2,3,4,5-tetrafluorobenzonitrile (**3b**), which ascertained the trifluorinated structure at the 2-, 3-, and 5-positions (Entry 3). Doubling the catalytic amount to 2 mol% led to a complete conversion and selectivity within 1 h. These results indicated that the C–F bond at the *para* position of the substituent was rather susceptible to the reduction [40,41].

Table 1. Synthesis of partially fluorinated arenes by catalytic transfer hydrogenative defluorination with HCOOK using **1** [1].

Entry	Substrate	HCOOK, eq	Time, h	% Yield [2]	
1	 **2a**	2	1	 **3a**, 100	
2	 **3a**	2	12	 **4**, 20	
3 [3]	 **3b**	2	2	 **4**, 100	
4 [4]	C_6F_6 **2b**	2	12	N.R.	
5	 **5a**	1	2	 **6a**, 7	 **7a**, 38
6	**5a**	3	2	**6a**, 0	**7a**, 99
7	 **5b**	1	1	 **6b**, 90(88) [5]	 **7b**, 2
8	**5b**	3	1	**6b**, 0	**7b**, 100(86) [5]
9	 **8a**	2	1	 **9a**, 100	
10	 **8b**	2	1	 **9b**, 98	

[1] Standard conditions: Substrate (0.5 mmol), **1** (5.0×10^{-3} mmol), 1,2-dimethoxyethane (2.5 mL), H_2O (2.5 mL), 30 °C. [2] Determined by ^{19}F NMR using trifluoromethylbenzene as an internal standard. [3] Catalyst loading = 2 mol%. [4] Catalyst loading = 5 mol%. [5] Isolated yield in parenthesis.

The lower reactivity of **3a** than that of **3b** accommodates the fact that C–F bonds at *para* positions are inherently unfavorable for the nucleophilic aromatic substitution mechanism. Considering the essential contribution of the negatively charged electronic structure at the *para* position of the carbon to which the nucleophile is introduced [42–48], the fluorine substituent at the *para* position possibly destabilizes the transition state due to the repulsion between the occupied p-orbital on the carbon and the lone electron pair on the fluorine (Scheme 3). Therefore, nucleophilic addition proceeds preferentially at the *para* position of substituents other than fluorine. Actually, ^{19}F NMR monitoring experiments of the HDF using 1 mol% of **1** revealed that hexafluorobenzene (**2b**) was intact in the presence of 3 equiv of HCOOK at 30 °C after 24 h (Entry 4 in Table 1).



Scheme 3. Destabilization by vicinal electron-pair repulsion through nucleophilic attack on the para position of a fluorine atom.

In the reaction of tetrafluoroterephthalonitrile (**5a**), which does not contain a fluorine atom at the *para* position of the cyano group, a monodefluorinated product (2,3,5-trifluoroterephthalonitrile; **6a**) was hardly obtained by the reduction with an equimolar amount of HCOOK (Entry 5). Alternatively, 2,5-difluoroterephthalonitrile (**7a**) was formed in a 38% yield as a result of the double defluorination. By using 3 equiv of HCOOK, **5a** was almost quantitatively converted into **7a** as a sole product after 2 h (Entry 6). The ^{19}F NMR analysis displayed a decay of the signal due to **5a** at −128 ppm, accompanied by the appearance of signals at −109 ppm and −119 ppm due to **7a** and potassium fluoride (see Figure S1 in the Supplementary Materials). The regiochemistry of the product was finally determined by X-ray crystallography, as shown in Figure 1 (left; a). These results indicated the comparatively smooth second defluorination at the *para* position of the initially incoming hydrogen atom.

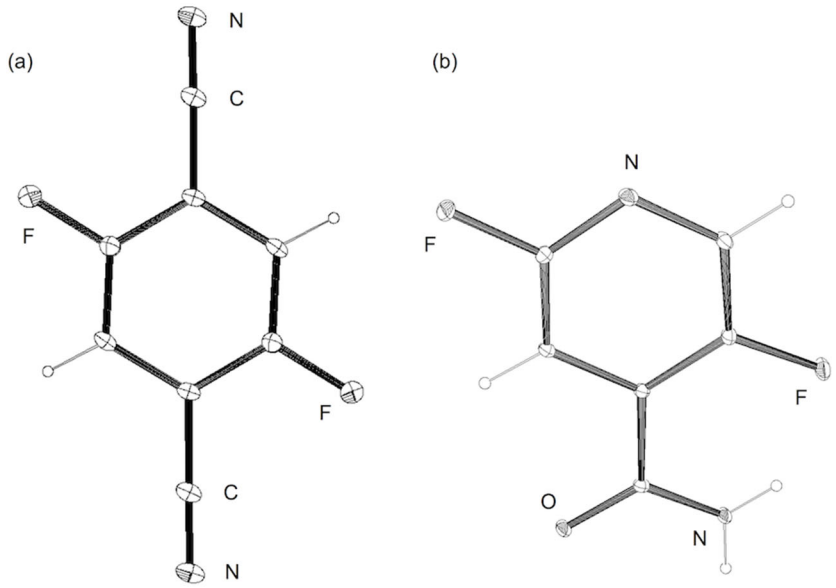
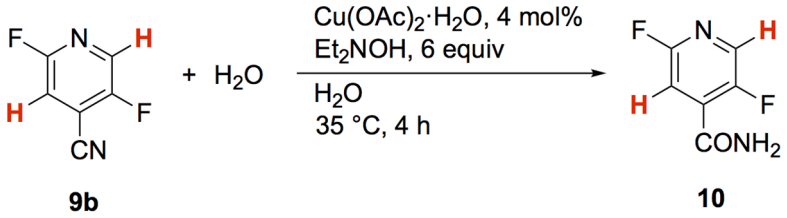


Figure 1. ORTEP drawings of **7a** (**left**; (**a**)) and **10** (**right**; (**b**)). Thermal ellipsoids are shown at the 30% probability level.

In contrast, the regioisomeric tetrafluorophthalonitrile (**5b**) can be reduced stepwise to give mono- and di-defluorinated products, as investigated in our previous work [33].

When **5b** was reduced with 1 equiv of HCOOK, the monosubstituted product, 3,4,6-trifluorophthalonitrile (**6b**), was successfully obtained in an 88% isolated yield (Entry 7). The HDF using 3 equiv of HCOOK afforded the corresponding consecutive transfer hydrogenation product (**7b**), in which the *para* positions of the two cyano groups were specifically defluorinated (Entry 8). The preferential *para* selectivity in the HDF of substituted perfluorobenzenes was substantiated by these experiments. The double-defluorinated product **7b** is the precursor of polyfluorinated phthalocyaninato complexes, which have been synthesized via six steps from 2,5-difluorobenzoyl chloride [49]. This selective HDF, enabling the synthesis of partially fluorinated compounds directly from perfluoroarenes, simplifies the conventional methods.

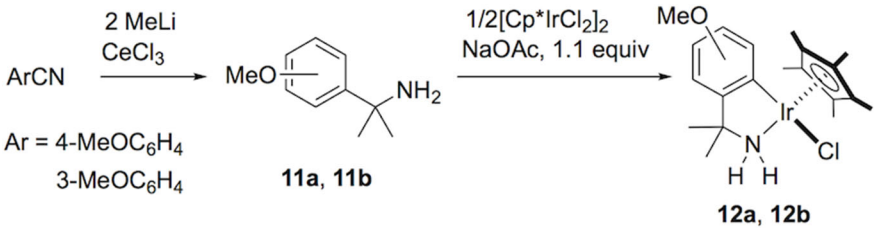
A reliable regioselectivity was also observed in the HDF of fluorinated pyridine derivatives [50]. In the HDF of 3-chloro-2,4,5,6-tetrafluoropyridine (**8a**) under standard conditions, the carbon–fluorine bond at the 4-position was specifically cleaved to yield 3-chloro-2,5,6-trifluoropyridine (**9a**) quantitatively without the erosion of the chlorine substituent (Entry 9). The monodefluorination in preference to dechlorination is a peculiar feature of the nucleophilic aromatic substitution mechanism [51], in contrast with the trend of aromatic hydrodehalogenation involving electron-transfer radical anion fragmentation, in which the heavier halogen favors undergoing fragmentation [52]. The reaction was also compatible with 4-cyano-2,3,5,6-tetrafluoropyridine (**8b**) possessing a non-fluorine substituent at the 4-position, leading to the formation of 4-cyano-2,5-difluoropyridine (**9b**) in a 98% yield via double defluorination with 2 equiv of HCOOK (Entry 10). As with the HDF of **5a** and **5b**, the high electron deficiency of the substrates allows for the consecutive substitution. This product was converted to the carboxamide derivative (**10**) by hydration in the presence of a copper catalyst (Scheme 4) [53], and the regiochemistry was determined by X-ray crystallographic analysis, as shown in Figure 1 (right).



9b **10**

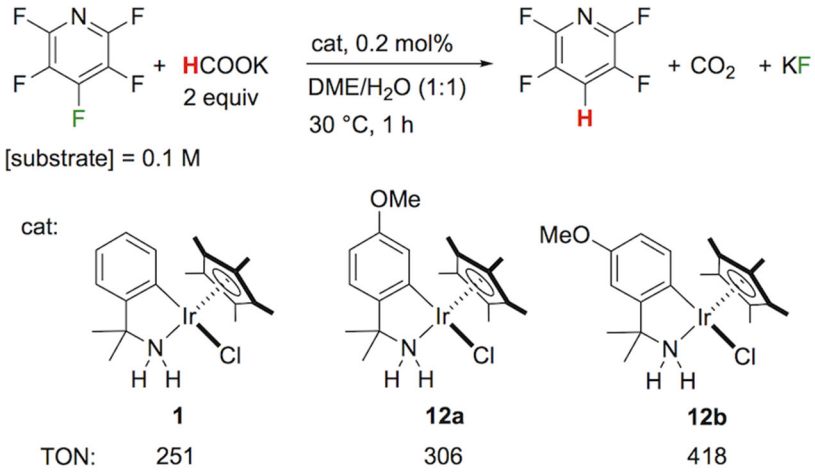
Scheme 4. $Cu(OAc)_2$-catalyzed hydration of **9b**.

Considering the important role of interim hydridoiridium species in the C–F bond cleavage, more nucleophilic iridium systems were used to facilitate the catalytic HDF. For the modified iridacycles, we examined the coordination of new C–N chelate ligands with electron-donating substituents (Scheme 5) and investigated their catalytic activity for the HDF. The cumylamine derivatives **11a** and **11b** were synthesized by a treatment of methylcerium with benzonitrile derivatives having a methoxy group at the *para* or *meta* position in THF [54]. In a similar manner to our original synthetic procedure for azairidacycles [55,56], orthometalation of **11a** was performed by mixing $[Cp^*IrCl_2]_2$ with sodium acetate (1 equiv/Ir) in acetonitrile at 60 °C for 10 h. After recrystallization, the expected chlorido complex (**12a**) was obtained as yellow crystals in a 73% yield (Scheme 5). For the transformation of 3-methoxy substituted analog **11b**, the metalation took place mainly at the 6-position, while a small amount of a sterically congested isomer was found in the crude products. After purification by chromatographic techniques, the major product **12b** was isolated.



Scheme 5. Synthesis of new azairidacycles **12a** and **12b**.

With the new azairidacycles, we further explored their catalytic activities for the transfer hydrogenative defluorination. The reaction of pentafluoropyridine with HCOOK (2 equiv) using the catalyst precursor **1** with a substrate/iridium ratio of 500 under otherwise standard conditions proceeded to give 2,3,5,6-tetrafluoropyridine with a turnover number of 251 after 1 h (Scheme 6). When **12a** was used as the catalyst, a slightly higher TON of 306 was obtained. By switching the catalyst with **12b**, a further enhancement of the catalytic activity was observed with a TON of 418. The complexes with a methoxy group on the aryl ligand showed an enhanced catalytic activity, possibly due to the electron-donating methoxy group improving the nucleophilicity of the catalytically active hydrido intermediate.



Scheme 6. Comparison of the catalytic activities of **1**, **12a**, and **12b** for the transfer hydrogenative defluorination of pentafluoropyridine with HCOOK.

In keeping with the attractive catalytic performance of **12b**, the double defluorination of **5b** was performed on a 1.1 g scale for 4 h with a substrate/catalyst ratio of 180. After purification by column chromatography, the desired product **7b** was successfully isolated in a 90% yield (0.81 g).

3. Materials and Methods

3.1. General Information

All manipulations of oxygen- and moisture-sensitive materials were performed under a purified argon atmosphere using standard Schlenk techniques. Solvents were purchased from Kanto Chemical Co., Inc. (Tokyo, Japan) and dried by refluxing over sodium benzophenone ketyl (THF, 1,4-dioxane, and diethyl ether), P_2O_5 (CH_3CN and CH_2Cl_2), or CaH_2 (2-propanol, pentane), and distilled under argon before use. Ethyl acetate and chloroform-d_1 was used as delivered. Dichloromethane-d_2 was degassed by three freeze-pump-thaw cycles and purified by trap-to-trap distillation after being dried with P_2O_5. The fluoroarene substrates were purchased from Kanto Chemical Co., Ltd. (Tokyo, Japan), Sigma-Aldrich Co. LLC. (St. Louis, MO, USA), Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan), and FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan), degassed, and

stored under argon atmosphere. The other reagents were purchased from Sigma-Aldrich Co. LLC. (St. Louis, MO, USA), Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan), and Nacalai Tesque Inc. (Kyoto, Japan), and used as delivered. The Ir catalyst **1** was prepared according to the procedures described in the literature [55]. ^{1}H (399.8 MHz), ^{19}F (376.2 MHz), and ^{13}C{^{1}H} (100.5 MHz) NMR spectra were recorded on a JNM-ECX400 spectrometer (JEOL Ltd., Tokyo, Japan) at around 25 °C. The NMR chemical shifts were referenced to an external tetramethylsilane signal (0.0 ppm) by using the signals of residual proton impurities in the deuterated solvents for ^{1}H and ^{13}C{^{1}H} NMR, and referenced to an external CF_3CO_2H signal (−76.5 ppm) for ^{19}F NMR. Recyclable preparative high-performance liquid chromatography was performed on an LC-9225 NEXT system (Japan Analytical Industry Co., Ltd., Tokyo, Japan) equipped with JAIGEL-1H and -2H columns using $CHCl_3$ as an eluent at a flow rate of 14 mL min^{-1}. Elemental analyses were carried out using a PE2400 Series II CHN analyzer (PerkinElmer, Inc., Waltham, MA, USA).

3.2. Representative Procedures of HDF of Fluoroarenes Using Potassium Formate under the Conditions of S/C = 100 at 30 °C

A mixture of the catalyst **1** (2.5 mg, 5.0 × 10^{-3} mmol), potassium formate (84.8 mg, 1.01 mmol), and pentafluorobenzonitrile (96.5 mg, 0.50 mmol) in 1,2-dimethoxyethane (2.5 mL) and water (2.5 mL) was stirred at 30 °C for 1 h. The product yield was determined by ^{19}F NMR spectroscopy using a solution of trifluoromethylbenzene (0.260 M) in 1,2-dimethoxyethane (1 mL) as an internal standard. After the HDF reaction, the compound was extracted by Et_2O (10 mL × 2) and was dried over $MgSO_4$. The catalysts were removed by filtration through a pad of Florisil. The sample after the evaporation was purified by silica gel column chromatography using hexane/ethyl acetate (with a ratio of 100/5–100/8) as the eluent.

3.3. Catalytic Hydration of **9b**

Copper(II) acetate (4.0 mg, 0.02 mmol), *N*,*N*-diethylhydroxylamine (292 mg, 3.27 mmol), and water were placed in a 20 mL reactor, and then **9b** (0.5 mmol) was added while stirring. After stirring the mixture at 35 °C for 4 h, the solvent was removed in vacuo, and the crude product was purified over a short pad of silica gel, eluted with CH_2Cl_2 and methanol (95:5). Colorless crystals of **10** suited for X-ray crystallography were obtained by recrystallization from CH_2Cl_2 and hexane.

3.4. Synthesis of **11a** *and* **11b**

Anhydrous $CeCl_3$ (0.84 g, 3.4 mmol) was stirred in dry THF (10 mL) at room temperature under Ar atmosphere for 2 h. The solution was cooled at −78 °C, and methyllithium (2.2 mL, 3.4 mmol, 1.6 M in diethyl ether) was added dropwise. After stirring the resulting mixture for 30 min at −78 °C, a solution of 4-methoxybenzonitrile (0.15 g, 1.1 mmol) in dry THF (5 mL) was added. The crude reaction mixture was stirred at room temperature overnight, quenched by adding 1.5 mL of concentrated ammonium chloride, and allowed to stir for 1 h at room temperature. The organic layer was filtered, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product of **11a** [57] was used for the next reaction without further purification.

Compound **11b** was obtained from 3-methoxybenzonitrile analogously to **11a** as a yellowish oil [58].

3.5. Synthesis of **12a**

To a mixture of $[Cp^*IrCl_2]_2$ (614.4 mg, 0.77 mmol) and NaOAc (128.6 mg, 1.57 mmol) in CH_3CN (15 mL), **11a** (254.7 mg, 1.54 mmol) was added. Then, the reaction mixture was stirred at 60 °C for 10 h. The solvent was removed under reduced pressure. The resulting reaction mixture in CH_2Cl_2 (10 mL) was washed with degassed water several times, and the organic layer was dried over Na_2SO_4. After removing insoluble materials by filtration, the evaporation of the filtrate to dryness gave a yellow powder. Further purification by

recrystallization from CH_2Cl_2 and ether gave orange crystals of **12a** in a 73% yield (591 mg, 1.12 mmol). ^{1}H NMR ($CDCl_3$, r.t., δ/ppm): δ 1.21 (s, 3H), 1.65 (s, 3H), 1.72 (s, 15H), 3.75 (br, 1H), 3.78 (s, 3H), 4.45 (br, 1H), 6.42 (dd, 1H; J = 2.6 and 8.4 Hz), 6.71 (d, 1H; J = 8.2 Hz), 7.06 (d, 1H; J = 2.7 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, r.t., δ/ppm): 9.3, 31.0, 31.9, 54.9, 65.8, 86.6, 107.5, 121.2, 121.6, 147.0, 154.8, 158.0. Anal. Calcd for [$C_{20}H_{29}ONClIr$]: C, 45.57; H, 5.55; N, 2.66; Found: C, 45.96; H, 5.40; N, 3.15%.

3.6. Synthesis of **12b**

To a mixture of [Cp*$IrCl_2$]$_2$ (1.003 g, 1.26 mmol) and NaOAc (273.2 mg, 3.34 mmol) in CH_3CN (50 mL), **11b** (427.3 mg, 2.59 mmol) was added. Then, the reaction mixture was stirred at 60 °C overnight. The solvent was removed under reduced pressure. The resulting reaction mixture in CH_2Cl_2 (10 mL) was washed with degassed water several times, and the organic layer was dried over Na_2SO_4. After removing insoluble materials by filtration, the evaporation of the filtrate to dryness gave a yellow powder. Recrystallization from CH_2Cl_2 and ether and subsequent purification by a preparative gel permeation chromatography gave an orange powder. Further purification by recrystallization from CH_2Cl_2 and ether gave orange crystals of **12b** in a 12% yield (158 mg, 0.30 mmol). ^{1}H NMR (CD_2Cl_2, r.t., δ/ppm): δ 1.18 (br, 3H), 1.62 (br, 3H), 1.68 (s, 15H), 3.71 (s, 3H), 3.85 (br, 1H), 4.36 (br, 1H), 6.39 (d, 1H; J = 2.8 Hz), 6.59 (dd, 1H; J = 2.8 and 8.2 Hz), 7.26 (d, 1H; J = 8.3 Hz). ^{13}C{^{1}H} NMR (CD_2Cl_2, r.t., δ/ppm): 9.1, 30.6, 31.5, 55.1, 66.2, 86.4, 108.1, 112.5, 136.3, 143.2, 155.4, 156.2. Anal. Calcd for [$C_{20}H_{29}ONClIr$]: C, 45.57; H, 5.55; N, 2.66; Found: C, 45.42; H, 5.34; N, 2.63%.

3.7. Scale-Up Experiment in the Synthesis of **7b**

A mixture of the catalyst **12b** (16.5 mg, 3.1×10^{-2} mmol), potassium formate (1.46 g, 17.2 mmol), and tetrafluorophthalonitrile (1.10 mg, 5.5 mmol) in 1,2-dimethoxyethane (25 mL) and water (25 mL) was stirred at 30 °C for 4 h. The mixture was extracted with Et_2O (20 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/ethyl acetate as the eluent to afford **7b** (0.81 g, 4.94 mmol, 90% yield) as a white solid.

3.8. X-ray Crystal Structure Determination

Diffraction experiments were performed on a Rigaku Saturn CCD area detector (Rigaku Corporation, Tokyo, Japan) using graphite-monochromated Mo-Kα radiation (λ = 0.71075 Å) under a nitrogen stream at 193 or 113 K (for **7a** and **10**, respectively). Single crystals suitable for X-ray analyses were mounted on glass fibers. The crystal-to-detector distance was 45.0 mm. Data were collected to a maximum 2θ value of 55.0°. A total of 720 oscillation images were collected. A sweep of the data was carried out by using ω scans from −110.0 to 70.0° in 0.5° steps at χ = 45.0° and ϕ = 0.0°. A second sweep was performed by using ω scans from −110.0 to 70.0° in 0.5° steps at χ = 45.0° and ϕ = 90.0°. Intensity data were collected for Lorentz-polarization effects and absorption. Details of the crystal and data collection parameters for the compounds **7a** and **10** are summarized in Table S1. The structure solution and refinements were performed with the CrystalStructure program package [59]. The heavy atom positions were determined by a direct program method (SIR92) [60], and the remaining non-hydrogen atoms were found by subsequent Fourier syntheses and were refined by full-matrix least-squares techniques against F^2 using the SHELXL-2014/7 program [61]. The hydrogen atoms were placed at calculated positions and were refined with a riding model.

4. Conclusions

In summary, this work expands on polyfluoroarene substrates for transfer hydrogenative defluorination catalyzed by the bifunctional iridium catalyst **1**. Based on the highly regioselective control in HDF, nucleophilic aromatic substitution is responsible for the C–F bond cleavage. A marked acceleration caused by the introduction of a methoxy group

into the azairidacycle structure corroborates the fact that the highly σ-donating nature of the iridium catalyst contributes to enhancing the hydridicity. These results will be of assistance in the design of new reduction catalyst systems with a metal/NH bifunctionality. In addition to practical reaction procedures that avoid hazardous reducing agents, the transfer hydrogenation system is characterized by an outstanding catalytic performance under mild conditions and thus offers further innovation opportunities for synthesizing a range of partially fluorinated aromatic compounds.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/org3030012/s1. Table S1: Crystallographic data for **7a** and **10**; Figure S1: HDF of **5a** Monitored by ^{19}F NMR Spectroscopy; Figures S2–S8: copies of ^{1}H and ^{13}C{^{1}H} NMR spectra of **10**, **12a**, and **12b**.

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